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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,733	05/02/2001	Michael Szardenings	1085.0050000/RWE	3759

7590 01/28/2004

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EXAMINER	
CHISM, BILLY D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,733	SZARDENINGS ET AL.	
	Examiner	Art Unit	
	B. Dell Chism	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64* is/are pending in the application.

4a) Of the above claim(s) *25,26,28 and 30-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,27 and 29* is/are rejected.

7)☒ Claim(s) *19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I in the response filed 03 November 2003 is acknowledged. The traversal is on the ground(s) that lack of unity existed between the groups and that dependent claims could not be grouped out since they are dependent upon claims in other Groups. Furthermore, Applicants argue that the lack of unity was improper since no prior art was cited. This is not found persuasive because the finding of lack of unity was expressed in paragraph 3, page 4 of the previous office action. The lack of unity is based on the fact that the Markush grouping for alternatives of chemical compounds of claim 1 was regarded as not being of similar nature since they did not meet both the criteria of 1) possessing a common property or activity; and 2) a common structure be present. In the present case, as explained in paragraph 3 page 4 of previous office action, the Markush grouping for alternatives of chemical compounds of claim 1 lack the first criteria of a common property or activity. As is indicated by the Applicants in claim 1, the compounds ***may or may not*** possess one or several properties listed in a)-d) of claim 1. On these grounds, unity lacks wherein there is no special technical feature. Consequently, with unity lacking, those Groups formed in the lack of unity, i.e., Group II drawn to DNA encoding a compound of general formula I, are considered separate inventions and will not be combined with the presently elected invention of Group I regardless of dependency. The Group II, as the other Groups, can stand-alone for patenting regardless of the structuring of the claim dependency. The examples stated by Applicants are those examples that define unity when the Markush grouping for alternative chemical compounds possess 1) a common property or activity; 2) a common structure be present, however, as indicated above and in the lack of unity, the present Markush grouping lacks a common property or activity as defined in claim 1.

Claim 30 is drawn to non-elected subject matter and will not be added to present Group I, however, claim 29 was omitted and is now considered as part of Group I.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-24, 27 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vitro selectivity studies for MC1 receptors, in vitro capacity to stimulate the second messenger cAMP, and in vitro nitric oxide inhibiton, does not reasonably provide enablement for the intended use of any compound of the formula I of claim 1 for in vivo use. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the

art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to the intended use of a compound of formula I of claim 1 for in vivo use. The specification (pages 3-52) teaches only in vitro use of a compound of formula 1 of claim 1 for in vitro selectivity and affinity studies for MC1 receptors, in vitro capacity to stimulate the second messenger cAMP, and in vitro nitric oxide inhibition.

The state of the prior art and the predictability or lack thereof in the art: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The art does not teach the compounds of formula 1 of claim 1 for in

vivo use. Szardenings *et al.* (J. of Biological Chemistry, Vol. 272, No. 44, pages 27943-27948) teach compounds similar in structure (Table III) as to those of formula I of claim 1, however, Szardenings *et al.* only teach in vitro uses for selectivity and affinity for MC1 receptors.

The amount of direction or guidance present and the presence or absence of working examples: Given the lack of teachings found in the art that the compounds of formula I of claim 1 can be used for in vivo purposes, detailed guidance is required in the specification to enable one of skill in the art to be able to use the claimed compounds for in vivo purposes. This guidance is absent. The specification contains only a vague disclosure that the compounds of claim 1 formula 1 can be used for in vivo immunomodulatory purposes, amelioration, prevention or inhibition of contact hypersensitivity and edema and inflammation of vessels and vasculitis, blood cell normalization, and inhibition of sensitization of a hapten. There is no guidance or working examples as how to administer a compound of claim 1 for in vivo use or what dosages would lead to amelioration, prevention or inhibition of those biological activities claimed in claims 13-20 or those intended uses for any of claims 1-24, 27 and 29. Furthermore, there is no guidance or working examples for the in vivo prevention of any of the claimed biological processes of claims 15, 18 and 19.

The breadth of the claims and the quantity of experimentation needed: Given the lack of teachings regarding the predictability for in vivo use of the claimed compounds, and in the absence of sufficient guidance in applicant's disclosure to overcome the lack of teachings in the art regarding predictability of in vivo use of the claimed compounds, it would require undue experimentation by one of skill in the art to be able to make and use the claimed invention.

4. Claim 27 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not give any guidance as to a fusion protein of any number of sequences of the compound of claim 1. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described and applied. They are:

1. The nature of the invention: presently Applicants are claiming a fusion protein comprising one or several copies of the sequence of claim 1.

2. The state of the prior art: the prior art does not teach a fusion protein comprising one or several copies of the sequence of the compound of claim 1.

3. The predictability or lack thereof in the art: there is absolutely no predictability even in view of the seemingly high level of skill in the art.

4. The amount of direction or guidance present: the specification merely mentions a fusion protein as an embodiment on page 14, however, offers no guidance or direction in how to make or use the fusion protein, i.e., when to use one or several copies of the sequence in claim 1.

5. The presence or absence of working examples: absent any working examples, one of skill in the art cannot be expected to see or predict the usefulness or efficacious nature of a fusion protein comprising one or several copies of the sequence of claim 1.

6. The breadth of the claim: the claim encompasses countless possibilities for fusion comprising one or several copies of the proteins.

7. The quantity of experimentation needed, and the level of the skill in the art: the quantity of experimentation needed would present an undue burden on one of skill in the art to make or use the claimed fusion protein with predictability since there is such breadth to the possible combinations and without working examples or proper guidance.

5. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not give any guidance as to a prodrug of any sequences of the compound of claim 1 for in vivo administration. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described and applied. They are:

1. The nature of the invention and the breadth of the claim: presently Applicants are claiming a prodrug comprising to be converted to the compound of claim 1 for in vivo administration. Consequently, the claim encompasses efficacious in vivo administration of a prodrug comprising a compound of claim 1.

2. The state of the prior art: the prior art does not teach a prodrug to be converted to a compound of claim 1for in vivo administration.

3. The predictability or lack thereof in the art: there is absolutely no predictability even in view of the seemingly high level of skill in the art for in vivo efficacy of a prodrug that is converted to a compound of claim 1 upon in vivo administration.

4. The amount of direction or guidance present: the specification merely mentions a prodrug as an embodiment on page 35, however, offers no guidance or direction in how to make or use the prodrug for in vivo administration.

5. The presence or absence of working examples: absent any working examples, one of skill in the art cannot be expected to see or predict the usefulness or efficacious nature of a prodrug comprising a compound of claim 1 for in vivo administration.

6. The quantity of experimentation needed, and the level of the skill in the art: without working examples or proper guidance, the quantity of experimentation needed would present an undue burden on one of skill in the art to make or use the claimed prodrug with predictability since there is such breadth to the claimed prodrug's efficacy.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 5, 8-9, 17 and 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites the limitation that the first amino acid at the N-terminus is to be a serine residue that has an OH of the CH_2. There is insufficient antecedent basis for this limitation in the claim because claim 5 is dependent upon formula I of claim 1 which does not provide for a hydroxyl containing group at the R19 position.

Claim 8 is rejected for the recitation of a range within in a range, wherein Applicant is listing the preferred ranges of those R numbers that they prefer to not be methyl.

Claims 9 and 10 are rejected for being drawn to non-elected subject matter, wherein the claims are drawn to compounds that are not encompassed by the limitations of formula I of Group I, claim 1, i.e., a serine at residue number one.

Claim 17 is rejected for the indefinite recitation of the term "effect" wherein it is unclear what "effect" a compound of claim 1 has on induction of a hapten, i.e., increase induction or decrease induction of a hapten.

Claim 27 is rejected wherein the claim is indefinite for whether the fusion protein can contain one copy of one of the possible sequences in claim and then contain several copies of other different sequences of claim 1 or if they are all to be the same or what order they should be or if order and/or sequence matters since the Applicants state in claim 1 that the different sequences comprise one or several different activities listed in claim 1 a)-d). The different possible activities for the different sequences make a fusion protein's activity indefinite.

Claim Objections

8. Claim 19 is objected to because of the following informalities: the term "vesseles" should read --vessels--. Appropriate correction is required.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to B. Dell Chism whose telephone number is 571-272-0962. The examiner can normally be reached on 7:30 AM - 4:30 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the

organization where this application or proceeding is assigned is 703-872-9306 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

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B. Dell Chism
20 January 2004

CHRISTOPHER R. TATE
PRIMARY EXAMINER